



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/574,084

05/15/2007

Elisabeth Bock

BOCK9

3782

1444 7590 07/24/2009  
BROWDY AND NEIMARK, P.L.L.C.  
624 NINTH STREET, NW  
SUITE 300  
WASHINGTON, DC 20001-5303

EXAMINER

NOAKES, SUZANNE MARIE

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

07/24/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/574,084	<b>Applicant(s)</b> BOCK ET AL.	
	<b>Examiner</b> SUZANNE M. NOAKES	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28,30-39 and 41-43 is/are pending in the application.
- 4a) Of the above claim(s) 1-7,30-39,42 and 43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8-28 and 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>01/03/2008</u>  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of Group II, claims 8-28 and 41 in the reply filed on 29 April 2009 is acknowledged. The traversal is on the ground(s) that one or more group II claims is allowable over the prior art and can serve as a basis for rejoinder. This is not found persuasive because until all pending and examined claims have been examined and are found allowable, rejoinder is not required. At such point that allowable subject matter should be found, the Examiner will notify Applicants.

The requirement is still deemed proper and is therefore made FINAL.

### ***Status of the Claims***

2. Claims 1-28, 30-39 and 41-43 are pending. Claims 1-7, 30-39, 42 and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **with** traverse as noted above. Thus, claims 8-28 and 41 are subject to examination.

### ***Priority***

3. The claim for benefit of priority of foreign application DK 2003 01417 filed 09/30/2003 is acknowledged.

***Information Disclosure Statement***

4. The information disclosure statement (IDS) submitted on 03 January 2008 has been considered by the examiner. See initialed and signed PTO-1449.

***Specification***

***Compliance with Sequence Rules***

5. The sequence listing, filed in computer readable form (CRF) and paper copy on 15 May 2007, has been received and entered. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

MPEP 2401.02 states:

The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. The rules apply to all sequences in a given application, whether claimed or not.

In the instant case, each .pdb file listed as Table 2, specifically defines more than four amino acids in a specific sequential order and thus said Table must identify the sequence disclosed therein. Including the appropriate SEQ ID NO: in the Table heading is sufficient for identification purposes and to overcome this objection.

Art Unit: 1656

\* If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

### ***Claim Objections***

6. Claims 8-28 and 41 are objected to because of the following informalities: In the first instance where an acronym is used in an independent claim, said acronym should be spelled out in full, followed by the abbreviation in parenthesis. Thus, in claim 8 NCAM should be spelled out as 'nuclear cell adhesion molecule (NCAM)'.

Appropriate corrections are required.

### ***Claim Rejections - 35 USC § 112 – 2<sup>nd</sup> paragraph***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 8 part (v) recites the limitation "wherein said peptide is selected by the method according to claim 20". There is insufficient antecedent basis for this limitation

Art Unit: 1656

in the claim because claim 20 is drawn to "The compound according to claim 8..."

Claims 9-28 and 41 are included in the instant rejection as they do not remedy the noted deficiency.

***Claim Rejections - 35 USC § 112 – 1<sup>st</sup> paragraph***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 8 and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to any compound, natural or non-natural which is capable of binding to the nuclear cell adhesion molecule (NCAM) homolyphic binding site which is composed of the Ig1, Ig2 and Ig3 molecules. Parts i-iv of claim 8 suggest that the compound can bind between the Ig1 and Ig3 molecules by binding somewhere on Ig1 (i); or somewhere on Ig3 (ii); or bind somewhere on Ig2 which would disrupt to the Ig2-Ig3 interaction (iii) or bind somewhere on Ig3 to disrupt the Ig2-Ig3 interaction (iv). Part (v) suggests the compound is a peptide of SEQ ID NO: 1-4, 7, 10-14, 16, 17, 18, 40 or 41 which binds to Ig2, or a fragment or variant thereof of any of these peptides.

However, the essence of the claims, especially parts i-iv of claim 8, is any kind of compound, naturally occurring or not, which can bind to NCAM homolyphic binding site of Ig1, Ig2 or Ig3 complex and disrupt said association, is plausible as long as it conforms to the three-dimensional structural requirements of any of the sites of Ig1, Ig2 or Ig3 association sites which is inherently defined by the Ig1-Ig2-Ig3 complex three-dimensional structure and conformation. Thus, the claims are drawn to a huge genus of compounds, naturally occurring or not, which are only defined by a three-dimensional structural conformation along with a limited function (e.g. they only need be capable of binding to the NCAM homolyphic binding site but need not do disrupt it, modulate the activity of the complex etc). However, what said non-naturally or naturally occurring compounds look like is not immediately discernable by one skilled in the art because there is no common structure required for said compounds, only that it binds said NCAM site (and thus fits in a semi-defined three-dimensional space imposed by said complex Ig1-Ig2-Ig3). However, given the variation of molecules which may fit into said space, there is no structure-function correlation. Thus, while the specification does define some selected species of compounds which are peptides as noted in dependent claims 9-28, these species are not deemed to be representative of the diverse genus of compounds wherein said compounds need only be required to bind but do not share a common structure whatsoever. One skilled in the art need only align the sequences of SEQ ID NOs: 1-18, 40 and 41 to see these species share no common structure. Furthermore, these peptides do not even touch on non-naturally occurring or naturally occurring organic small molecules which also may be capable of binding.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that 'the inventor invented the claimed invention.' *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ('[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'). Thus, an applicant complies with the written description requirement 'by describing the invention, with all its claimed limitations, not that which makes it obvious,' and by using 'such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.' *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does



state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

While the specification describes how to find various compounds which fit into the large and variable genus of compounds being claimed by performing *in vitro* assays (see for example pp. 26-29) or of utilizing the protein crystal or crystal structure of the Ig1-2-3 complex to perform *in silico* analysis (see for example, pp. 29-45 and 45-50), it is noted that this is insufficient to claim the instant genus. The courts have established that possession, in terms of written description, may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. Analogously, one cannot describe all chemical compounds, natural or not, based upon a pharmacophore (e.g. three-dimensional constraints of space such as those imposed by the Ig1-2-3 complex) wherein the compound is not required to have even a single common structural feature among the members of the species.

Thus, it is asserted that Applicant's are claiming a generic class of molecules, which is a huge genus essentially of unrelated molecules that do not have a structure function correlation, rather just a defined function. Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the broad scope of the genus as claimed.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 8-10, 12-14, 16, 17, 19-26 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by NCBI Accession polypeptide as first submitted by Small et al. (J. Cell Biol. 105:2335-2345 (1987) and identified as P13596.

Small et al. teach the identification of the full length NCAM polypeptide from rat. Said sequence is 100% identical to the instant SEQ ID NOs: 1, 2, 4-6, 8, 9 and 11-26.

It is noted that the limitations of the indicated claims and the recitation of “having” is interpreted as being open comprising language. Thus, said polypeptide as taught by Small et al./NCBI Accession P13596 is asserted to inherently be capable of binding to the NCAM homolyphic binding site composed of Ig1-2-3.

Art Unit: 1656

**SEQ ID NO: 1 (P13596 – Small et al. – numbering reflects P13596)**

RESULT 2

NCAM1\_RAT

**ID NCAM1 RAT Reviewed; 858 AA.****AC P13596;****DT 01-JAN-1990, integrated into UniProtKB/Swiss-Prot.****DT 01-JAN-1990, sequence version 1.**

DT 25-NOV-2008, entry version 91.

DE RecName: Full=Neural cell adhesion molecule 1;

DE Short=NCAM-1;

DE Short=N-CAM-1;

DE AltName: CD\_antigen=CD56;

DE Flags: Precursor;

GN Name=Ncam1; Synonyms=Ncam;

OS Rattus norvegicus (Rat).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi;

OC Muroidea; Muridae; Murinae; Rattus.

OX NCBI\_TaxID=10116;

RN [1]

RP NUCLEOTIDE SEQUENCE [MRNA].

RC TISSUE=Brain;

RX MEDLINE=88059265; PubMed=3680385; DOI=10.1083/jcb.105.5.2335;

**RA Small S.J., Shull G.E., Santoni M.-J., Akeson R.;****RT "Identification of a cDNA clone that contains the complete coding****sequence for a 140-kD rat NCAM polypeptide.";****RL J. Cell Biol. 105:2335-2345(1987).**

RN [2]

RP NUCLEOTIDE SEQUENCE OF 340-381.

RX MEDLINE=91035620; PubMed=1699951; DOI=10.1083/jcb.111.5.2089;

RA Small S.J., Akeson R.;

RT "Expression of the unique NCAM VASE exon is independently regulated in  
RT distinct tissues during development.";

RL J. Cell Biol. 111:2089-2096(1990).

RN [3]

RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 355-364.

RX MEDLINE=90166485; PubMed=2483093; DOI=10.1016/0896-6273(88)90158-4;

RA Small S.J., Haines S.L., Akeson R.A.;

RT "Polypeptide variation in an N-CAM extracellular immunoglobulin-like  
RT fold is developmentally regulated through alternative splicing.";

RL Neuron 1:1007-1017(1988).

RN [4]

RP PROTEIN SEQUENCE OF 38-48 AND 594-605, AND MASS SPECTROMETRY.

RC STRAIN=Sprague-Dawley; TISSUE=Brain;

RA Lubec G., Kang S.U.;

RL Submitted (JUL-2007) to UniProtKB.

CC -!- FUNCTION: This protein is a cell adhesion molecule involved in  
CC neuron-neuron adhesion, neurite fasciculation, outgrowth of  
CC neurites, etc.CC -!- SUBCELLULAR LOCATION: Cell membrane; Single-pass type I membrane  
CC protein.

## Art Unit: 1656

CC    -!- ALTERNATIVE PRODUCTS:  
CC        Event=Alternative splicing; Named isoforms=1;  
CC        Comment=A number of isoforms are produced;  
CC        Name=1; Synonyms=N-CAM 140;  
CC        IsoId=P13596-1; Sequence=Displayed;  
CC    -!- SIMILARITY: Contains 2 fibronectin type-III domains.  
CC    -!- SIMILARITY: Contains 5 Ig-like C2-type (immunoglobulin-like)  
CC        domains.  
CC    -----  
CC    Copyrighted by the UniProt Consortium, see <http://www.uniprot.org/terms>  
CC    Distributed under the Creative Commons Attribution-NoDerivs License  
CC    -----  
DR    EMBL; X06564; CAA29809.1; -; mRNA.  
DR    EMBL; M32611; AAA41679.1; -; Genomic\_DNA.  
DR    PIR; S00846; IJRTNC.  
DR    RefSeq; NP\_113709.1; -.  
DR    UniGene; Rn.11283; -.  
DR    PDB; 1EPF; X-ray; 1.85 A; A/B/C/D=20-208.  
DR    PDB; 1LWR; NMR; -; A=612-705.  
DR    PDB; 1QZ1; X-ray; 2.00 A; A=20-308.  
DR    PDBsum; 1EPF; -.  
DR    PDBsum; 1LWR; -.  
DR    PDBsum; 1QZ1; -.  
DR    SMR; P13596; 509-609.  
DR    Ensembl; ENSRNOG00000031890; Rattus norvegicus.  
DR    GeneID; 24586; -.  
DR    KEGG; rno:24586; -.  
DR    RGD; 67378; Ncam1.  
DR    HOVERGEN; P13596; -.  
DR    LinkHub; P13596; -.  
DR    NextBio; 603762; -.  
DR    ArrayExpress; P13596; -.  
DR    GermOnline; ENSRNOG00000031890; Rattus norvegicus.  
DR    GO; GO:0016021; C:integral to membrane; IEA:UniProtKB-KW.  
DR    GO; GO:0005886; C:plasma membrane; IEA:UniProtKB-KW.  
DR    GO; GO:0008201; F:heparin binding; IEA:UniProtKB-KW.  
DR    GO; GO:0005515; F:protein binding; IEA:UniProtKB-KW.  
DR    GO; GO:0007155; P:cell adhesion; IEA:InterPro.  
DR    InterPro; IPR008957; Fibronectin\_typ-III-like\_fold.  
DR    InterPro; IPR003961; FN\_III.  
DR    InterPro; IPR013151; Ig.  
DR    InterPro; IPR007110; Ig-like.  
DR    InterPro; IPR013783; Ig-like\_fold.  
DR    InterPro; IPR013098; Ig\_I-set.  
DR    InterPro; IPR003598; Ig\_sub2.  
DR    InterPro; IPR009138; Neural\_cell\_adh.  
DR    Gene3D; G3DSA:2.60.40.30; FN\_III-like; 1.  
DR    Gene3D; G3DSA:2.60.40.10; Ig-like\_fold; 5.  
DR    Pfam; PF00041; fn3; 2.  
DR    Pfam; PF07679; I-set; 2.  
DR    Pfam; PF00047; ig; 3.  
DR    PRINTS; PR01838; NCAMFAMILY.  
DR    SMART; SM00060; FN3; 2.  
DR    SMART; SM00408; IGc2; 5.

## Art Unit: 1656

DR PROSITE; PS50853; FN3; 2.  
 DR PROSITE; PS50835; IG\_LIKE; 5.  
 PE 1: Evidence at protein level;  
 KW 3D-structure; Alternative splicing; Cell adhesion; Cell membrane;  
 KW Direct protein sequencing; Glycoprotein; Heparin-binding;  
 KW Immunoglobulin domain; Membrane; Phosphoprotein; Repeat; Signal;  
 KW Transmembrane.  
 FT SIGNAL 1 19 By similarity.  
 FT CHAIN 20 858 Neural cell adhesion molecule 1.  
 FT /FTId=PRO\_0000015015.  
 FT TOPO\_DOM 20 721 Extracellular (Potential).  
 FT TRANSMEM 722 739 Potential.  
 FT TOPO\_DOM 740 858 Cytoplasmic (Potential).  
 FT DOMAIN 20 111 Ig-like C2-type 1.  
 FT DOMAIN 116 205 Ig-like C2-type 2.  
 FT DOMAIN 212 302 Ig-like C2-type 3.  
 FT DOMAIN 309 414 Ig-like C2-type 4.  
 FT DOMAIN 417 502 Ig-like C2-type 5.  
 FT DOMAIN 507 606 Fibronectin type-III 1.  
 FT DOMAIN 608 702 Fibronectin type-III 2.  
 FT REGION 152 156 Heparin-binding (Potential).  
 FT REGION 161 165 Heparin-binding (Potential).  
 FT MOD\_RES 784 784 Phosphoserine (By similarity).  
 FT CARBOHYD 222 222 N-linked (GlcNAc . .) (Potential).  
 FT CARBOHYD 316 316 N-linked (GlcNAc . .) (Potential).  
 FT CARBOHYD 348 348 N-linked (GlcNAc . .) (Potential).  
 FT CARBOHYD 434 434 N-linked (GlcNAc . .) (Potential).  
 FT CARBOHYD 460 460 N-linked (GlcNAc . .) (Potential).  
 FT CARBOHYD 489 489 N-linked (GlcNAc . .) (Potential).  
 FT DISULFID 41 96 By similarity.  
 FT DISULFID 139 189 By similarity.  
 FT DISULFID 235 288 By similarity.  
 FT DISULFID 330 396 By similarity.  
 FT DISULFID 437 490 By similarity.  
 FT STRAND 22 32  
 FT STRAND 37 43  
 FT STRAND 51 55  
 FT STRAND 65 75  
 FT STRAND 78 83  
 FT HELIX 88 90  
 FT STRAND 92 99  
 FT STRAND 105 115  
 FT STRAND 118 122  
 FT STRAND 125 128  
 FT STRAND 135 137  
 FT STRAND 140 142  
 FT STRAND 148 153  
 FT HELIX 158 161  
 FT STRAND 166 168  
 FT STRAND 174 176  
 FT HELIX 181 183  
 FT STRAND 185 193  
 FT HELIX 194 196  
 FT STRAND 198 207

Art Unit: 1656

```

FT   STRAND      209    217
FT   STRAND      219    224
FT   STRAND      231    241
FT   STRAND      244    249
FT   STRAND      262    266
FT   STRAND      272    275
FT   HELIX       280    282
FT   STRAND      284    292
FT   STRAND      295    306
FT   STRAND      616    622
FT   TURN        623    626
FT   STRAND      627    633
FT   STRAND      637    639
FT   STRAND      642    654
FT   STRAND      667    673
FT   STRAND      679    688
FT   STRAND      691    701
SQ   SEQUENCE    858 AA;  94658 MW;  EA1A06A4EA0550F6 CRC64;

```

```

Query Match          100.0%;  Score 76;  DB 1;  Length 858;
Best Local Similarity 100.0%;  Pred. No. 0.00066;
Matches 13;  Conservative 0;  Mismatches 0;  Indels 0;  Gaps
0;

```

```

Qy          1 WFSPNGEKLSPNQ 13
             |||||
Db          54 WFSPNGEKLSPNQ 66

```

**SEQ ID NO: 2 (P13596 – Small et al.)**

```

Query Match          100.0%;  Score 76;  DB 1;  Length 858;
Best Local Similarity 100.0%;  Pred. No. 0.00066;
Matches 13;  Conservative 0;  Mismatches 0;  Indels 0;  Gaps
0;

```

```

Qy          1 WFSPNGEKLSPNQ 13
             |||||
Db          54 WFSPNGEKLSPNQ 66

```

**SEQ ID NO: 4 (P13596 – Small et al.)**

```

Qy          1 QIRGIKKT 9
             |||||
Db          175 QIRGIKKT 183

```

**SEQ ID NO: 5 (P13596 – Small et al.)**

```
Qy          1  DVR  3
            |||
Db          162 DVR 164
```

**SEQ ID NO: 6 (P13596 – Small et al.)**

```
Qy          1  RGIKKT 7
            |||||
Db          178 RGIKKT 183
```

**SEQ ID NO: 8 (P13596 – Small et al.)**

```
Qy          1  KEGED 5
            ||||
Db          130 KEGED 134
```

**SEQ ID NO: 9 (P13596 – Small et al.)**

```
Qy          1  IRGIKKT 8
            |||||
Db          176 IRGIKKT 183
```

**SEQ ID NO: 11 (P13596 – Small et al.)**

```
Qy          1  DKNDE 5
            ||||
Db          279 DKNDE 283
```

**SEQ ID NO: 12 (P13596 – Small et al.)**

```
Qy          1  TVQARNSIVNAT 12
            |||||
Db          213 TVQARNSIVNAT 224
```

**SEQ ID NO: 13 (P13596 – Small et al.)**

```
Qy          1 SIHLKVFAK 9
             |||||
Db          300 SIHLKVFAK 308
```

**SEQ ID NO: 14 (P13596– Small et al.)**

```
Qy          1 LSNNYLQIR 9
             |||||
Db          179 LSNNYLQIR 186
```

**SEQ ID NO: 15 (P13596 – Small et al.)**

```
Qy          1 RFIVLSNNYLQIR 13
             |||||
Db          175 RFIVLSNNYLQIR 186
```

**SEQ ID NO: 16 (P13596 – Small et al.)**

```
Qy          1 KKDVRFIVLSNNYLQIR 17
             |||||
Db          171 KKDVRFIVLSNNYLQIR 186
```

**SEQ ID NO: 17 (P13596 – Small et al.)**

```
Qy          1 QEFKEGEDAVIV 12
             |||||
Db          127 QEFKEGEDAVIV 138
```

**SEQ ID NO: 18 (P13596– Small et al.)**



Art Unit: 1656

Qy                    1 KEGEDAVIVCD 11  
                      | | | | | | | | | |  
Db                130 KEGEDAVIVCD 140

### ***Conclusion***

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/

Application/Control Number: 10/574,084

Page 17

Art Unit: 1656

Primary Examiner, Art Unit 1656

22 July 2009